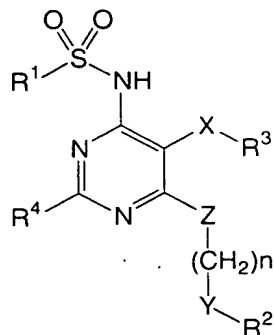


**AMENDMENTS TO THE CLAIMS (INCLUDING PRESENTATION OF NEW CLAIMS):**

This listing of claims will replace all prior versions of claims in the application.

**Claims:**

1. (Currently amended) Compounds of the general formula I:



**General Formula I**

wherein

**R<sup>1</sup>** represents lower alkyl;

**R<sup>2</sup>** represents aryl; heteroaryl; lower alkyl;

**R<sup>3</sup>** represents aryl; heteroaryl;

**R<sup>4</sup>** represents hydrogen; trifluoromethyl; lower alkyl; lower alkyl-amino; lower alkoxy; lower alkoxy-lower alkoxy; hydroxy-lower alkoxy; lower alkyl-sulfinyl; lower alkylthio; lower alkylthio-lower alkyl; hydroxy-lower alkyl; lower alkoxy-lower alkyl; hydroxy-lower alkoxy-lower alkyl; hydroxy-lower alkyl-amino; lower alkyl-amino-lower alkyl; amino; di-lower alkyl-amino; [N-(hydroxy-lower alkyl)-N-(lower alkyl)]-amino; aryl; aryl-amino; aryl-lower alkyl-amino; aryl-thio; aryl-lower alkyl-thio; aryloxy; aryl-lower alkoxy; aryl-lower alkyl; aryl-sulfinyl; heteroaryl; heteroaryl-oxy; heteroaryl-lower alkyl-oxy; heteroaryl-

amino; heteroaryl-lower alkyl-amino; heteroaryl-thio; heteroaryl-lower alkyl-thio; heteroaryl-lower alkyl; heteroaryl-sulfinyl; heterocyclyl; heterocyclyl-lower alkoxy; heterocyclyl-oxy; heterocyclyl-amino; heterocyclyl-lower alkyl-amino; heterocyclyl-thio; heterocyclyl-lower alkyl-thio; heterocyclyl-lower alkyl; heterocyclyl-sulfinyl; cycloalkyl; cycloalkyl-oxy; cycloalkyl-lower alkoxy; cycloalkyl-amino; cycloalkyl-lower alkyl-amino; cycloalkyl-thio; cycloalkyl-lower alkyl-thio; cycloalkyl-lower alkyl; cycloalkyl-sulfinyl;

**X** represents oxygen; or a bond;

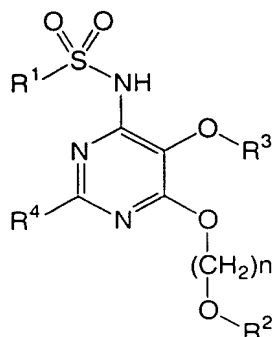
**Y** represents oxygen; -NH-; -NH-SO<sub>2</sub>-; -NH-SO<sub>2</sub>-NH-; -O-CO-NH-; -NH-CO-O-; or -NH-CO-NH-;

**Z** represents oxygen; sulfur; or -NH-;

**n** represents an integer selected from 2; 3; or 4;

~~and~~ or optically pure enantiomers or diastereomers, mixtures of enantiomers or diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates ~~and~~ or the meso-forms and pharmaceutically acceptable salts thereof.

2. (Currently Amended) The Compounds compounds of Claim 1 having of the formula  
II :



**Formula II**

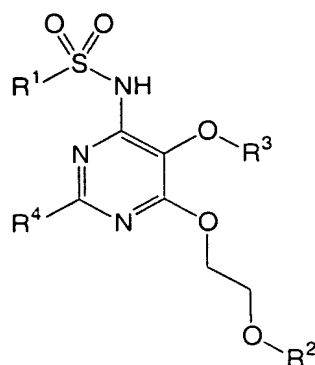
wherein

**R<sup>1</sup>** represents ethyl; propyl; iso-propyl; or butyl;

**R<sup>2</sup>** represents aryl; or heteroaryl;

and **R<sup>3</sup>**, **R<sup>4</sup>** and **n** are as defined in general formula I above and or optically pure enantiomers or diastereomers, mixtures of enantiomers or diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates and the meso-forms and or pharmaceutically acceptable salts thereof.

3. (Currently Amended) The Compounds compounds of Claim 2 having of the formula  
III:



**Formula III**

wherein

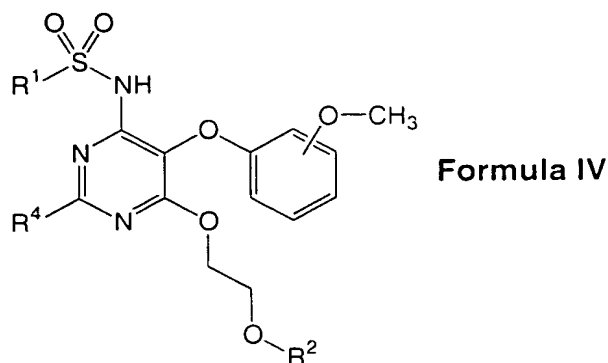
**R¹** represents ethyl; propyl; or butyl;

**R²** represents aryl; or heteroaryl;

**R⁴** represents hydrogen; or heteroaryl;

and **R³** is as ~~defined in general formula I above~~ and or optically pure enantiomers or diastereomers, mixtures of enantiomers or diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates ~~and~~ or the meso-forms and pharmaceutically acceptable salts thereof.

4. (Currently Amended) The Compounds compounds of Claim 3 having the formula IV  
:



wherein

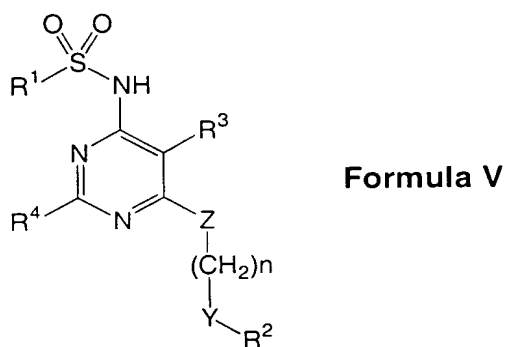
$R^1$  represents ethyl; propyl; iso-propyl; or butyl;

$R^2$  represents aryl; or heteroaryl

$R^4$  represents hydrogen; or heteroaryl;

and or optically pure enantiomers or diastereomers, mixtures of enantiomers or diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates and the meso-forms and or pharmaceutically acceptable salts thereof.

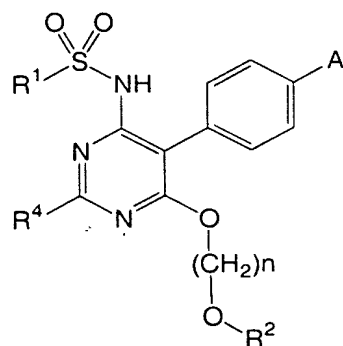
5. (Currently Amended) The Compounds compounds of Claim 1 having ~~of the formula~~  $\Psi$ :



wherein

$R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  as well as Y, Z and n are as defined in general formula I above and or optically pure enantiomers or diastereomers, mixtures of enantiomers or diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates and the meso-forms ~~and~~ or pharmaceutically acceptable salts thereof.

6. (Currently Amended) The Compounds compounds of Claim 5 having ~~of the formula VI:~~



**Formula VI**

wherein

$R^1$  represents ethyl; propyl; or butyl;

$R^2$  represents aryl; or heteroaryl;

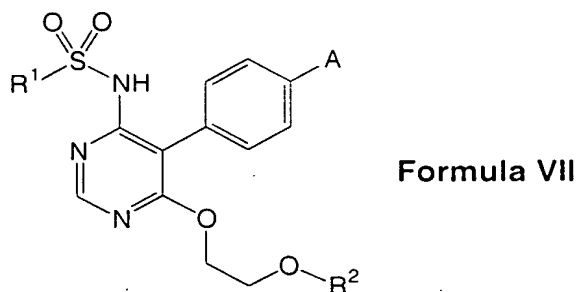
$R^4$  represents hydrogen or heteroaryl;

A represents hydrogen; methyl; ethyl; chlorine; or bromine;

and n represents the integers 2; or 3;

~~and~~ or optically pure enantiomers or diastereomers, mixtures of enantiomers or diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates and the meso-forms ~~and~~ or pharmaceutically acceptable salts thereof.

7. (Currently Amended) ~~The Compounds~~ compounds of Claim 6 having the formula VII:



wherein

**R<sup>1</sup>** represents ethyl; propyl; or butyl;

**R<sup>2</sup>** represents heteroaryl;

**A** represents methyl; chlorine; or bromine;

~~and~~ or optically pure enantiomers or diastereomers, mixtures of enantiomers or diastereomers, diastereomeric racemates, mixtures of diastereomeric racemates ~~and~~ or the meso-forms and pharmaceutically acceptable salts thereof.

8. (Currently Amended) ~~The compounds selected from claims 1 to 7 of~~ Claim 1  
selected from the group consisting of

Ethanesulfonic acid {6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-p-tolyl-pyrimidin-4-yl}-amide;

n-Propanesulfonic acid {6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-p-tolyl-pyrimidin-4-yl}-amide;

Ethanesulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(4-chloro-phenyl)-pyrimidin-4-yl]-amide;

n-Propanesulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(4-chloro-phenyl)-pyrimidin-4-yl]-amide;

Ethanesulfonic acid {5-(4-bromo-phenyl)-6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl}-amide;

n-Propanesulfonic acid {5-(4-bromo-phenyl)-6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl}-amide;

Ethanesulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-methoxy-phenoxy)-[2,2']bipyrimidinyl-4-yl]-amide;

n-Propanesulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-methoxy-phenoxy)-[2,2']bipyrimidinyl-4-yl]-amide;

Ethanesulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-methoxy-phenoxy)-pyrimidin-4-yl]-amide;

n-Propanesulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-methoxy-phenoxy)-pyrimidin-4-yl]-amide;

N-[6-[2-(5-Bromo-pyrimidin-2-yloxy)-ethoxy]-5-p-tolyl-pyrimidin-4-yl]-methanesulfonamide;

Ethanesulfonic acid [5-(2-chloro-5-methoxy-phenoxy)-6-[2-(5-methylsulfanyl-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl]-amide;

Butane-1-sulfonic acid [5-(3-methoxy-phenoxy)-6-[2-(5-methylsulfanyl-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl]-amide;

Ethanesulfonic acid [5-(4-bromo-phenyl)-6-[2-(5-methylsulfanyl-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl]-amide;



Propane-1-sulfonic acid [5-(2-chloro-5-methoxy-phenoxy)-6-[2-(5-methylsulfanyl-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl]-amide;

~~and~~ or pharmaceutically acceptable salts thereof.

9. (Currently Amended) ~~The compound selected from claims 1 to 7~~ of claim 1 selected from the group consisting of:

N-[5-(4-Bromo-phenyl)-6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl]-methanesulfonamide;

Ethanesulfonic acid [5-(4-bromo-phenyl)-6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl]-amide;

Propane-1-sulfonic acid [5-(4-bromo-phenyl)-6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl]-amide;

Propane-1-sulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-methoxy-phenoxy)-pyrimidin-4-yl]-amide;

Ethanesulfonic acid [6-[2-(5-methylsulfanyl-pyrimidin-2-yloxy)-ethoxy]-5-p-tolyl-pyrimidin-4-yl]-amide;

Propane-1-sulfonic acid [5-(4-bromo-phenyl)-6-[2-(5-methylsulfanyl-pyrimidin-2-yloxy)-ethoxy]-pyrimidin-4-yl]-amide;

Ethanesulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-chloro-5-methoxy-phenoxy)-pyrimidin-4-yl]-amide;

Propane-1-sulfonic acid [6-[2-(5-bromo-pyrimidin-2-yloxy)-ethoxy]-5-(2-chloro-5-methoxy-phenoxy)-pyrimidin-4-yl]-amide;

~~and~~ or pharmaceutically acceptable salts thereof.

Claims 10-17 (cancelled).

18. (Currently Amended) A composition comprising a ~~The use of one or more compounds of any one of claims 1 to 9 as active ingredients for the production of pharmaceutical compositions~~ for the treatment of disorders associated with a role of endothelin.

19. (Currently Amended) A composition comprising a ~~The use of one or more compounds of any one of claims 1 to 9 as active ingredients for the production of pharmaceutical compositions~~ for the treatment of circulatory disorders which are associated with a role of endothelin.

20. (Currently Amended) A composition comprising a ~~The use of one or more compounds of any one of claims 1 to 9 as active ingredients for the production of pharmaceutical compositions~~ for the treatment of inflammatory disorders which are associated with a role of endothelin.

21. (Currently Amended) A composition comprising a ~~The use of one or more compounds of any one of claims 1 to 9 as active ingredients for the production of pharmaceutical compositions~~ for the treatment of proliferative disorders which are associated with a role of endothelin.

22. (Currently Amended) A composition comprising a ~~The use of one or more compounds of any one of claims 1 to 9 as active ingredients for the production of pharmaceutical compositions~~ for the treatment of hypertension, coronary diseases, cardiac insufficiency, renal and myocardial ischemia, renal failure, cerebral ischemia, dementia, migraine, subarachnoidal hemorrhage, Raynaud's syndrome, portal hypertension, pulmonary hypertension, atherosclerosis, prevention of restenosis after balloon or stent angioplasty, inflammation, pulmonary fibrosis, connective tissue diseases, stomach and duodenal ulcer, digital ulcer, cancer, melanoma, prostatic cancer, prostatic hypertrophy, erectile dysfunction, hearing loss, amaurosis, chronic

bronchitis, asthma, gram negative septicemia, shock, sickle cell anemia, glomerulonephritis, renal colic, glaucoma, therapy and prophylaxis of diabetic complications, complications of vascular or cardiac surgery or after organ transplantation, ~~and~~ or complications of cyclosporin.

23. (Currently Amended) A composition comprising a ~~The use of one or more~~ compounds of ~~any one of~~ claims 1 ~~to 9~~ as active ingredients in combination with one or more other substances therapeutically useful for the treatment of hypertension, coronary diseases, cardiac insufficiency, renal and myocardial ischemia, renal failure, cerebral ischemia, dementia, migraine, subarachnoidal hemorrhage, Raynaud's syndrome, portal hypertension, pulmonary hypertension, atherosclerosis, prevention of restenosis after balloon or stent angioplasty, inflammation, pulmonary fibrosis, connective tissue diseases, stomach and duodenal ulcer, digital ulcer, cancer, melanoma, prostatic cancer, prostatic hypertrophy, erectile dysfunction, hearing loss, amaurosis, chronic bronchitis, asthma, gram negative septicemia, shock, sickle cell anemia, glomerulonephritis, renal colic, glaucoma, therapy and prophylaxis of diabetic complications, complications of vascular or cardiac surgery or after organ transplantation, ~~and~~ or complications of cyclosporin.

24. (Currently Amended) A process for the manufacture of pharmaceutical compositions for the treatment of disorders associated with a role of endothelin containing ~~one or more~~ compounds ~~as claimed in any one of~~ claims 1 ~~to 9~~ as active ingredients which process comprises mixing one or more active ingredients with pharmaceutically acceptable excipients ~~in a manner known per se~~.

25. (Newly Presented) A method of treating disorders associated with a role of endothelin, comprising administering to the patient in need of said treatment, a compound of Claim 1 in an effective amount to treat said disorder.

26. (Newly Presented) A method of treating circulatory disorders associated with a role of endothelin, comprising administering to the patient in need of said treatment, a compound of Claim 1 in an effective amount to treat said disorder.

27. (Newly Presented) A method of treating inflammatory disorders associated with a role of endothelin, comprising administering to the patient in need of said treatment, a compound of Claim 1 in an effective amount to treat said disorder.

28. (Newly Presented) A method of treating proliferative disorders associated with a role of endothelin, comprising administering to patient in need of said treatment, a compound of Claim 1 in an effective amount to treat said disorders.

29. (Newly Presented) A method of treating disorders selected from the group consisting of hypertension, coronary diseases, cardiac insufficiency, renal and myocardial ischemia, renal failure, cerebral ischemia, dementia, migraine, subarachnoidal hemorrhage, Raynaud's syndrome, portal hypertension, pulmonary hypertension, pulmonary hypertension, atherosclerosis, prevention of restenosis after balloon or stent angioplasty, inflammation, pulmonary fibrosis, connective tissue diseases, stomach and duodenal ulcer, digital ulcer, cancer, prostatic hypertrophy, erectile dysfunction, hearing loss, amaurosis, chronic bronchitis, asthma, gram negative septicemia, shock, sickle cell anemia, glomerulonephritis, renal colic, glaucoma, complications of vascular or cardiac surgery or after organ transplantation, and complications of cyclosporin, therapy and prophylaxis of diabetic complications, comprising of administering to patient in need of said treatment a compound of Claim 1 in an effective amount to treat said disorder.

30. (Newly Presented) A method for the treatment of disorders which are associated with a role of endothelin, and require mixed ET<sub>A</sub> and ET<sub>B</sub> blocking for treatment,

comprising administering to patient in need of said treatment a compound of Claim 1 in an effective amount to treat said disorders.

31. (Newly Presented) A method for the treatment of disorders which are associated with a role of endothelin, and require selective ET<sub>A</sub> blocking for treatment, comprising administering to patient in need of said treatment a compound of Claim 1 in an effective amount to treat said disorder.

32. (Newly Presented) A method for the treatment of disorders requiring selective ET<sub>B</sub> blocking for treatment, comprising administering to patient in need of said treatment a compound of Claim 1 in an effective amount to treat said disorders.

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